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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/229,226 | 01/12/1999 | JIN LIU | GTRC-1957 | 7360 |

7590 09/13/2002

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EXAMINER

SMITH, RUTH S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

3737

DATE MAILED: 09/13/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/229,226

Applicant(s)

LIU ET AL.

Examiner

Ruth S Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 July 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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Claim Rejections - 35 USC § 112

Claims 1-25,27-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is vague and indefinite in that it is unclear as to how the step set forth on lines 3-4 differs from the step set forth in claim 27, lines 4-5. It appears that such a step is redundant in view of the limitation set forth in claim 27. The preamble of claim 1 is inconsistent with the preamble of claim 27. Claim 27 is vague and indefinite in that reference to a different tissue on line 7 implies that a first tissue has been previously set forth, however, such a term lacks antecedent basis in that the preamble refers to tissue in the alternative only. Claims 31-33 appear to be inconsistent with the limitation set forth in claim 27 regarding applying the transducer to a site other than where transport or cell viability is to be altered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-2,10,11,14,15,17,19,21,23-28 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Klopotek (6,113,559). The claims are directly readable on Klopotek which discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. The ultrasound is applied to the other layers of skin and affect cells in the underlying layers of skin. The underlying

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layers of skin are considered to be different tissue at a second distant site. With regard to claims 19,21, the feedback signals used regarding cavitation are measured at frequencies as set forth in the claims.

Claims 27-28,30 are rejected under 35 U.S.C. 102(b) as being anticipated by Eppstein et al. The claims are directly readable on Eppstein et al which disclose the use of ultrasound energy to alter transport of agents into the body. The frequency can be changed such that the energy is directed to a deeper part of the tissue. Therefore, the energy is administered at the skin by a transducer placed thereon and the energy alters transport and cell viability at a site distant from the layer of skin on which the transducer is placed. The site distant from the layer of skin on which the transducer is placed comprises different tissue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Klopotek ('559). Klopotek discloses using a feedback system to modify continued application of ultrasound for the treatment of tissue. The feedback system measures properties such

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as ultrasound energy levels, temperature etc. In the absence of any showing of criticality, the means used to analyze the energy measurements would have been an obvious design choice of known equivalents in the art.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bommannan in view of Klopotek ('559). Bommannan et al disclose administering acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The energy is administered for a time period which can be selected based upon the drug administered, and the disease or injury treated (see column 7, lines 6-10). The measurement of the time that the ultrasound is applied is a measurement of a property of the acoustic energy. Klopotek discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have provided a feedback system as taught by Klopotek to monitor the treatment time and end treatment after the desired time has passed or other parameters of the applied energy in order to avoid harming the patient.

Claims 1-5,8-18,23-26,29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eppstein et al in view of Klopotek ('559). Eppstein et al disclose administering acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The frequency and/or intensity can be selected based upon the drug administered, and the disease or injury treated. Klopotek discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have provided a feedback system as taught by Klopotek in order to avoid transmitting excessive waves through the patient. With respect to claim 3, the agent passed through the membrane would have been an obvious selection based upon the intended treatment, and in the form of an emulsion or liposome as is well known. With regard to claim 9, it appears that such is an inherent function of the method. With regard to

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claims 13,29, it appears that the method of Eppstein et al would be applicable to any type of biological membrane and to any type of cell. With regard to claim 14, Eppstein et al disclose a frequency in the range of .1-100MHz. With respect to claim 16, in the absence of any showing of criticality, the peak positive pressure used would have been obvious to one skilled in the art without undue experimentation in order to achieve the desired result. With regard to claim 17, the step is an inherent result of the method. With regard to claims 23,24, the frequency and device location can be changed depending upon the procedure being performed.

Claim 1-3,5,7,14,15,18,23,25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tachibana et al in view of Klopotek ('559). Tachibana et al disclose the use of low-level ultrasound to alter cell viability. The ultrasound is administered for a predetermined time period after which it is terminated. The intensity was varied over time and the ultrasound was used to kill cells. The ultrasound was applied at a frequency of 270 KHz and used with agent such as Photofrin II. Klopotek discloses using a feedback system to modify continued application of low-level ultrasound for the treatment of tissue. Klopotek uses a non-invasive ultrasound device that is placed against the skin to apply ultrasound to underlying layers of skin. The underlying layers of skin are considered to be different tissue at a second distant site. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have modified Tachibana et al such that it includes a non-invasive low-level ultrasound device and a feedback system as taught by Klopotek in order to ensure that the treatment is being performed as desired and without causing harm to the patient. The use of the device as disclosed by Klopotek involves the selection of a well known ultrasound device for in-vivo low-level ultrasonic treatment.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eppstein et al in view of Bommannan et al. Eppstein et al disclose the use of ultrasound energy to alter transport of agents across the stratum corneum. Eppstein et al further disclose that the ultrasound can be controlled to enhance the transdermal molecular flux rate

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either into or out of the human body. The frequency can be changed such that the energy is directed to a deeper part of the tissue. Therefore, the energy is administered at the skin by a transducer placed thereon and the energy alters transport and cell viability at a site distant from the layer of skin on which the transducer is placed. The site distant from the layer of skin on which the transducer is placed comprises different tissue. Bommannan et al disclose administering acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The energy is administered for a time period which can be selected based upon the drug administered, and the disease or injury treated (see column 7, lines 6-10). The measurement of the time that the ultrasound is applied is a measurement of a property of the acoustic energy. Bommannan et al further disclose that the method can be used to sample and evaluate biological fluids in the body (see column 4, lines 55-59). It would have been obvious to one skilled in the art to have modified Eppstein et al such that in addition to transporting drugs into the body, the ultrasound is selected to enhance the transdermal molecular flux rate out of the human body and used to evaluate biological fluids in the body. The advantage of such is to monitor the effect of the drug treatment.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ogden in view of Klopotek ('559). Ogden discloses administering acoustic energy to skin or other biological membrane in order to alter the permeability of the membrane. The frequency and/or intensity can be selected based upon the drug administered, and the disease or injury treated. Ogden discloses that the frequency and treatment time can be changed. A feedback loop is used to monitor drug delivery amounts and temperature and the treatment is affected by such measurements. Klopotek discloses using a feedback system to modify continued application of ultrasound to the underlying layers of skin. The feedback system measures properties such as ultrasound energy levels, temperature etc. It would have been obvious to one skilled in the art to have provided a feedback means as taught by Klopotek to monitor the treatment time and

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intensity/frequency used and modify treatment based upon the monitored parameter in order to avoid transmitting excessive waves through the patient as set forth in column 6.

Allowable Subject Matter

Claims 20,31-33 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Response to Arguments

Applicant's arguments filed July 24, 2002 have been fully considered but they are not persuasive. The underlying layers of skin are considered to be different tissue at a second distant site.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth S Smith whose telephone number is 308-3063. The examiner can normally be reached on M-F 5:30AM -2:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marvin Lateef can be reached on 308-3256. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3590 for regular communications and (703) 308-0758 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-0858.



Ruth S Smith
Primary Examiner
Art Unit 3737

RSS
September 12, 2002